

## **REMARKS**

### **I. Status of the Claims**

Claims 2-6, 8-13, 23-26, and 102 were examined and rejected by the Office. In accordance with the Examiner Interview of July 28, 2009, the Applicants respectfully request entry and consideration of the attached declaration of Dr. Christopher Knight and Dr. Julia Dibner. The Applicants respectfully submit that the claims are in condition for allowance, and respectfully solicit allowance of all pending claims.

### **II. Summary of the Claimed Invention**

The currently claimed invention recites methods for isolating a viable oocyst using a hydrocyclone. Nowhere in the prior art has it been disclosed, taught, or suggested that a hydrocyclone could be used to separate a viable oocyst. "The use of a hydrocyclone . . . was previously believed to fatally damage the oocysts due to intense sheer forces."<sup>1</sup>

### **III. 35 U.S.C. § 103 Rejections**

***(a) Pending claims 2-6, 8-10, and 23-26 are not rendered obvious by Conkle et al. in view of Singh et al.***

Reconsideration is requested of the rejection of claims 2-6, 8-10, and 23-26 under 35 U.S.C. § 103(a) under Conkle *et al.* ("Conkle") in view of Singh *et al.* (Singh).<sup>2</sup>

Three criteria must be present to establish a *prima facie* case of obviousness.<sup>3</sup> First, the prior art reference must teach or suggest all the claim limitations. Second, there must be some reason for one of ordinary skill in the art to modify or combine the reference(s). Third, there must be a reasonable expectation of success.<sup>4</sup> These three criteria are not satisfied by Conkle and Singh, either alone or in combination.

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<sup>1</sup> Paragraph [0084], Originally Filed Patent Specification.

<sup>2</sup> Conkle *et al.*, WO 2000/50072; Singh *et al.* (1995) Cereal Chemistry 72(4):344-348.

<sup>3</sup> MPEP §2143.

<sup>4</sup> *Id.*

In the Office Action it is asserted that Conkle "suggest the use of other methods of processing oocysts to eliminate the use of harsh chemicals such as potassium dichromate." As provided by the attached declaration of Dr. Knight and Dr. Dibner, the use or non-use of potassium dichromate is unrelated to the use or non-use of a hydrocyclone.

"The Office Action further states at page 7 that Conkle *et al.* "... suggest the use of other methods of processing oocysts to eliminate the use of harsh chemicals such as potassium dichromate." This is not technically correct, first, because Conkle still uses potassium dichromate as an oxidizing agent at page 8, line 6 of Conkle, such that potassium dichromate would still be present in their vaccine. Secondly, and more importantly, potassium dichromate is used for its biostatic/oxidizing ability (*i.e.*, to minimize bacterial growth within the remaining fecal matter), not for oocyst isolation. There is no relationship between potassium dichromate and new methods of separation/isolation. Thus, there is no relationship between potassium dichromate and the use or non-use of a hydrocyclone. Rather, as mentioned previously, there were a number of factors that made us initially believe that using a hydrocyclone would not be effective at isolating a viable oocyst for making a live-vaccine."<sup>5</sup>

Consequently, the attached declaration makes clear that the Conkle reference does not provide any reason or motivation to isolate a viable oocyst with a hydrocyclone, as recited by the currently claimed invention. Without a reason or motivation to combine, the *prima facie* case under § 103 has been rebutted.

The attached declaration also provides evidence that, at the time of filing, a skilled artisan would have had no reasonable expectation of success in combining the recited elements in the manner currently claimed. In particular, the declaration recites that oocysts were fragile and susceptible to rupture. Because the hydrocyclone applied extreme sheer forces, it was suspected that the oocysts would be destroyed by the use of a hydrocyclone.

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<sup>5</sup> Declaration of Dr. Christopher D. Knight and Dr. Julia J. Dibner, at paragraph 7, submitted herewith.

"Through our employment at Novus as indicated above, we both are familiar with and have supervised portions of the research and development efforts that resulted in the discovery of the methods currently claimed in the '391 application. At the outset of the project, we were skeptical that hydrocyclones could be used to isolate viable oocysts. To be useful for the production of a live-vaccine, the oocysts are required to be viable following isolation. Oocysts, however, were known in the art to be extremely fragile and destroyed by agitation, stirring, or even by the mechanical action of digestion. See, e.g., newly identified supporting references showing the general state of the art, including U.S. Patent No. 4,808,404 ("The sporozoites of *Elimeria* species once out of their protective shells, i.e., oocysts and sporocysts, are very fragile and lose their infectivity within a few days."); U.S. Patent No. 6,891,024 ("Oocysts and sporocysts are found in the intestinal contents but the fragile oocyst is commonly disrupted by the time feces are passed."); and U.S. Patent No. 6,998,126 ("The wall of the sporulated oocyst is ruptured by the mechanical action in the gizzard and intestinal tract . . ."). Our experience at Novus International in handling oocysts further confirms that they are extremely fragile and subject to rupture."<sup>6</sup>

As provided by the above, to be useful for the production of the live-vaccine, the oocysts had to remain "viable," and the use of a hydrocyclone was thought likely to destroy the oocysts. In fact, the information provided by the declaration is further supported by the Conkle reference, which states, "Overall, the agitation level should be . . . not enough to destroy the oocysts. This may occur through aeration, shaking, stirring, and combinations thereof." (See WO 00/50072 at page 7, line 31-37). In view of the above, it is respectfully asserted that the currently claimed methods provide unexpected results with respect to viable oocysts.

The Office Action specifically acknowledges that, "Conkle *et al.* do not teach hydrocyclones." See Office Action, page 7, line 10. Singh use a hydrocyclone to separate starch particles from protein particles in a solution of wet-milled corn. Nowhere does the Singh reference disclose or suggest that a hydrocyclone could be

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<sup>6</sup> *Id* at paragraph 4.

successfully used to separate and/or isolate "viable" oocysts. Singh compared the use of a hydrocyclone to separate fractionated starch from wet-milled corn with the traditional starch tabling procedure (*i.e.*, the use of long (~20 feet) sloped tables that allow starch granules to settle by gravity such that they can be separated from the liquid phase). While the advantages cited by Singh may be significant for starch, they are not relevant to the methods used to separate "viable" oocysts from a liquid suspension, as required by the method of claims 2-6, 8-10, and 23-26. Thus, it is asserted that Singh is non-analogous art because it provides no disclosures whatsoever regarding a "viable" oocyst.

The Office's citation of *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), is not applicable to the current case because the currently claimed invention did not combine "familiar elements" to "yield predictable results." See Office Action, page 8, lines 1-5. The attached declaration of Dr. Knight and Dr. Dibner shows that the results were surprising and unexpected – not predictable.

"Thus, in the initial stages of the project resulting in the '391 application, we were skeptical that a hydrocyclone could be used to isolate a viable oocyst since hydrocyclones apply extreme sheer forces, which we thought were likely to destroy the oocysts. Hydrocyclones had not been previously used to isolate oocysts. At the time, our only knowledge of the use of hydrocyclones was for the removal of waste products, for example, in mining or other industrial applications. There were no positive indications for using a hydrocyclone to separate oocysts, particularly when the oocysts needed to be viable."<sup>7</sup>

"A *prima facie* case of obviousness may be rebutted by showing that the prior art, in any material way, teaches away from the claimed invention." *In re Geisler*, 116 F.3d 1465, 1471; 43 USPQ2d 1362, 1366 (Fed. Cir. 1997). "When the prior art teaches away from combining certain known elements, discovery of successful means of combining them is more likely to be nonobvious." *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007). Applicants respectfully assert that there was no motivation to

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<sup>7</sup> *Id* at paragraph 5.

modify/combine the references as proposed by the Office and, alternatively, no reasonable expectation of success in arriving at Applicants' claimed invention as required by § 103. Consequently, the Applicants respectfully assert that the *prima facie* case of obviousness has been rebutted. In view of the foregoing, the Applicants respectfully request withdrawal of the obviousness rejections of pending claims 2-6, 8-10, and 23-26 under Conkle in view of Singh.

***(b) Claims 11-13 are not rendered obvious in view of Conkle, Singh, and in further view of Sjoerdsma et al.***

Reconsideration is requested of the rejection of claims 11-13 under 35 U.S.C. § 103(a) in view of Conkle, Singh, and in further view of Sjoerdsma *et al.* ("Sjoerdsma").<sup>8</sup>

Claims 11-13 each require use of a hydrocyclone to separate "viable" oocysts. For all of the reasons detailed in section (a) and the accompanying declaration, use of a hydrocyclone to separate "viable" oocysts as required by claims 11-13 is not obvious in view of the cited art. The above arguments from section (a) are hereby incorporated by reference and reasserted herein.

The defect in the Office Action's obviousness rejection is not cured by resort to Sjoerdsma, either alone or in combination with Conkle and Singh. The Office Action states that, "Sjoerdsma *et al.* teach that mesh screens can be used to extract debris from biological material." Importantly, Sjoerdsma does not refer to the separation of any viable oocysts, but only a mixture of 2-difluoromethyl-2,5-diaminopentanoic acid, corn starch, lactose, and zinc stearate. Sjoerdsma also does not disclose, teach, or suggest use of a hydrocyclone to separate "viable" oocysts. The reference only discloses that mesh screens can be used to extract debris from a starch paste (See Sjoerdsma, Example 6, column 24, lines 28-34).

Applicants respectfully assert that there was no motivation to modify/combine the references as proposed by the Office and, alternatively, no reasonable expectation of success in arriving at Applicants' claimed invention as required by § 103.

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<sup>8</sup> Conkle *et al.*, WO 2000/50072; Singh *et al.* (1995), *Cereal Chemistry* 72(4):344-348; Sjoerdsma *et al.*, U.S. Patent No. 4,399,151, published August 16, 1983.

Consequently, the Applicants respectfully assert that the *prima facie* case of obviousness has been rebutted. In view of the foregoing, the Applicants respectfully request withdrawal of the obviousness rejections of pending claims 11-13 under Conkle, Singh, and in further view of Sjoerdsma.

***(c) Claim 102 is not rendered obvious in view of Conkle and Singh, as applied to claims 2-6, 8-10, and 23-26 above, and in further view of Kimura et al.***

Reconsideration is requested of the rejection of claim 102 under 35 U.S.C. § 103(a) in view of Conkle, Singh, as applied to claims 2-6, 8-10, and 23-26 above, and in further view of Kimura *et al.* ("Kimura").<sup>9</sup>

Claim 102 requires use of a hydrocyclone to separate "viable" oocysts. For all of the reasons detailed in section (a) and the accompanying declaration, use of a hydrocyclone to separate viable oocysts as required by claim 102 is not obvious in view of the cited art. The above arguments from section (a) are hereby incorporated by reference and reasserted herein.

The defect in the Office's obviousness rejection is not cured by resort to Kimura, either alone or in combination with Conkle and Singh. The Office Action states that "Kimura *et al* teach a flotation technique using sucrose (see the Abstract). . ." However, as with the other cited art, Kimura fails to disclose, teach, or suggest any use of a hydrocyclone to separate "viable" oocyst, as currently claimed.

Applicants respectfully assert that there was no motivation to modify/combine the references as proposed by the Office and, alternatively, no reasonable expectation of success in arriving at Applicants' claimed invention as required by § 103. Consequently, the Applicants respectfully assert that the *prima facie* case of obviousness has been rebutted. In view of the foregoing, the Applicants respectfully request withdrawal of the obviousness rejections of pending claim 102 under Conkle, Singh, and Kimura, either alone or in combination.

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<sup>9</sup> Conkle *et al.*, WO 2000/50072; Singh *et al.* (1995), *Cereal Chemistry* 72(4):344-348; Kimura *et al.*, *Journal of Protozoology Research*, July 2000, vol. 10, No. 3, pp. 155-165 (Abstract only).

**(d) Claims 2-6, 8-10, and 23-26 are not rendered obvious under Conkle in view of Alesina et al.**

Reconsideration is requested of the new rejection of claims 2-6, 8-10, and 23-26 under 35 U.S.C. § 103(a) under Conkle in view of Alesina et al. ("Alesina").

Claims 2-6, 8-10, and 23-26 require use of a hydrocyclone to separate "viable" oocysts. For all of the reasons detailed in section (a) and the accompanying declaration, use of a hydrocyclone to separate viable oocysts as required by claims 2-6, 8-10, and 23-26 is not obvious in view of the cited art. The above arguments from section (a) are hereby incorporated by reference and reasserted herein.

The defect in the Office's obviousness rejection is not cured by resort to Alesina, either alone or in combination with the other cited references. It is asserted by the Office that Alesina teaches "hydrocyclones can be used for microorganism suspension and separation." See Office Action, page 18, lines 6-7. As noted by the attached declaration, however, the term "microorganism" is not an art-based equivalent for the term "oocyst" – there are a number of physical and structural differences. Furthermore, the Alesina reference does not discuss whether the microorganisms are live or dead before or after separation. Specifically, the declaration provides the following:

"In the recent Office Action concerning the '391 application, mailed on June 24, 2009, the Patent Office cites to a new reference referred to as Alesina et al. (SU 19984621763; "Alesina"). The abstract provided of Alesina refers to a hydrocyclone for use in microorganism suspension separation. The reference, however, makes no mention whether the microorganism suspension would be live or dead before or after separation. Furthermore, the term "microorganism" is not an art-recognized equivalent of oocysts, since oocysts are more akin to fertilized eggs, which are not yet developed enough to be infective. Physically, oocysts are also much larger and less dense than microorganisms such as bacteria, including structural differences in the outer membrane/cell wall that make oocysts substantially more fragile than bacteria. Consequently, oocysts would not be considered to be the

same or substantially similar to the term "microorganisms" as  
set forth by the Patent Office."<sup>10</sup>

In view of the above, the Applicants respectfully assert that there was no motivation to modify/combine the references as proposed by the Office and, alternatively, no reasonable expectation of success in arriving at Applicants' claimed invention as required by § 103. Consequently, the Applicants respectfully assert that the *prima facie* case of obviousness has been rebutted. In view of the foregoing, the Applicants respectfully request withdrawal of the obviousness rejections of pending claim 102 under Conkle in view of Alesina, either alone or in combination.

**(e) Claims 11-13 are not rendered obvious under Conkle, Alesina, and further in view of Sjoerdsma.**

Reconsideration is requested of the new rejection of claims 11-13 under 35 U.S.C. § 103(a) under Conkle, Alesina, and further in view of Sjoerdsma. For all of the reasons detailed in sections (a)-(d) and the accompanying declaration, use of a hydrocyclone to separate "viable" oocysts as required by claims 11-13 is not obvious in view of the cited art. The above arguments from sections (a)-(d) are hereby incorporated by reference and reasserted herein. The Applicants respectfully assert that the *prima facie* case of obviousness has been rebutted.

**(f) Claim 102 is not rendered obvious under Conkle, Alesina, Sjoerdsma, and further in view of Kimura**

Reconsideration is requested of the new rejection of claim 102 under 35 U.S.C. § 103(a) under Conkle, Alesina, Sjoerdsma, and further in view of Kimura. For all of the reasons detailed in sections (a)-(e) and the accompanying declaration, use of a hydrocyclone to separate "viable" oocysts as required by claim 102 is not obvious in view of the cited art. The above arguments from sections (a)-(e) are hereby

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<sup>10</sup> *Id* at paragraph 6.



incorporated by reference and reasserted herein. The Applicants respectfully assert that the *prima facie* case of obviousness has been rebutted.

#### **IV. Conclusion**

In light of the foregoing, the Applicants respectfully request entry of the remarks and the attached declaration, and further solicit an allowance of all pending claims, *i.e.*, claims 2-6, 8-10, 23-26, and 102. The Commissioner is hereby authorized to charge any and all fees that may be required or credit any overpayment to Deposit Account No. 50-1662.

Polsinelli Shughart PC  
Respectfully Submitted,

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By: /J. Morgan Kirley/  
J. Morgan Kirley, Reg. No. 59,089

On Behalf of  
Kathryn J. Doty, Registration No. 40,593  
100 South Fourth Street, Suite 1100  
St. Louis, Missouri 63102  
Tel: (314) 889-8000  
Fax: (314) 231-1776  
Attorney for Applicant